

REMARKS

I. Status Summary

Claims 1-30 are pending in the present application and are currently examined. Claims 6, 9, 15, 23, 26 and 30 are herein cancelled. Claims 1-3, 5, 7, 8, 10-12, 14, 16-22, 24, 25 and 27-29 are herein amended.

The Examiner has made an objection to claim 28 for a typographical error. In addition, claims 1-30 are rejected under 35 U.S.C. § 101 as allegedly failing to recite a tangible result. Claims 1-30 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claims 1-30 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to enable a person of skill in the art to use the invention. The Examiner has rejected claims 1-3, 6-12, 15-20, and 23-30 under 35 U.C.S. § 102(a) as allegedly being anticipated by journal article to Van der Laan et al. (*Biostatistics*, December 2001, Vol. 2(4): pages 445-461; hereinafter "Van der Laan"). The Examiner has rejected claims 1-30 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Van der Laan in view of U.S. Patent Application Publication No. 2003/0219797 to Zhao et al. (hereinafter "Zhao").

II. Claim Amendments

Claim 1 is amended beginning at line 3 by the insertion of the phrase "for a given gene over a variety of experimental conditions." Claim 1 is amended at line 7 by insertion of the phrase as follows: "wherein the significance scores are outputted to a memory". In addition, claim 1 is amended at line 10 to recite the selecting of gene expression level measurements having a predefined significance score rather than selecting based on its significance score. Claim 1 is amended for clarity beginning at line 13 to recite: "to determine the non-overlapping parameter(s) present in the selected gene expression level measurements but not present in the non-selected gene expression level measurements". Claim 1 is amended at the end by addition of the phrase: "wherein the function of the gene(s) can be inferred based on the non-overlapping parameters". Claim 1 is amended throughout to replace the term "said" with the term "the". Support for these amendments can be found throughout the claims

and specification as filed and, in particular, at page 7, lines 13-14; page 3, lines 2-4; at page 4, lines 6-9; original claim 6; page 3, lines 16-17; page 3, lines 19-23; and page 3, lines 23-24. Accordingly, no impermissible new matter has been added by this claim amendment.

Claims 2-5, 7, and 8 are amended for clarity to replace the term "said" with the term "the". Claim 5 is further amended to recite a plurality of gene expression level measurements rather than a single measurement. Claim 8 is further amended for clarity by deletion of the redundant phrase: "of said gene expression level measurements". Support for these amendments can be found throughout the claims and specification as filed. Accordingly, no impermissible new matter has been added by this claim amendment.

Claim 10 is amended beginning at line 4 to recite assembling a distribution of gene expression level measurements for a given gene over a variety of experimental conditions," and at line 8 by insertion of the phrase as follows: "wherein the significance scores are outputted to a memory". In addition, claim 10 is amended at line 11 to recite the selecting of gene expression level measurements having a predefined significance score rather than selecting based on its significance score. Claim 10 is amended for clarity beginning at line 14 to recite: "to determine the non-overlapping parameter(s) present in the selected gene expression level measurements but not present in the non-selected gene expression level measurements". Claim 10 is amended at the end by addition of the phrase: "wherein the function of the gene can be inferred based on the non-overlapping parameters". Claim 10 is amended throughout to replace the term "said" with the term "the". Support for these amendments can be found throughout the claims and specification as filed and, in particular, at page 7, lines 13-14; page 3, lines 2-4; at page 4, lines 6-9; original claim 6; page 3, lines 16-17; page 3, lines 19-23; and page 3, lines 23-24. Accordingly, no impermissible new matter has been added by this claim amendment.

Claims 11, 12, 14, 16, and 17 are amended for clarity to replace the term "said" with the term "the" and to correct typographical errors. Claim 14 is further amended to recite a plurality of gene expression level measurements rather than a single measurement. Claim 17 is further amended for clarity by deletion of the redundant

phrase: "of said gene expression level measurements". Support for these amendments can be found throughout the claims and specification as filed. Accordingly, no impermissible new matter has been added by this claim amendment.

Claim 18 is amended at line 2 to correct the typographical error in using the term "method" instead of "system." Claim 18 is also amended at line 4 to recite the phrase "for a given gene over a variety of experimental conditions." Claim 18 is amended at line 7 by insertion of the phrase as follows: "wherein the significance scores are outputted to a memory". In addition, claim 18 is amended at line 10 to recite the selecting of gene expression level measurements having a predefined significance score rather than selecting based on its significance score. Claim 18 is amended for clarity beginning at line 13 to recite: "to determine the non-overlapping parameter(s) present in the selected gene expression level measurements but not present in the non-selected gene expression level measurements". Claim 18 is amended at the end by addition of the phrase: "wherein the function of the gene can be inferred based on the non-overlapping parameters". Claim 18 is amended throughout to replace the term "said" with the term "the". Support for these amendments can be found throughout the claims and specification as filed and, in particular, at page 7, lines 13-14; page 3, lines 2-4; at page 4, lines 6-9; original claim 6; page 3, lines 16-17; page 3, lines 19-23; and page 3, lines 23-24. Accordingly, no impermissible new matter has been added by this claim amendment.

Claims 19-22, 24, and 25 are amended for clarity to replace the term "said" with the term "the" and to correct typographical errors. Claim 22 is further amended to recite a plurality of gene expression level measurements rather than a single measurement. Claim 25 is further amended for clarity by deletion of the redundant phrase: "of said gene expression level measurements". Support for these amendments can be found throughout the claims and specification as filed. Accordingly, no impermissible new matter has been added by this claim amendment.

Claim 27 is amended at line 9 to recite the phrase "for a given gene over a variety of experimental conditions." Claim 27 is amended at line 12 by insertion of the phrase as follows: "wherein the significance scores are outputted to a memory". In addition, claim 27 is amended at line 15 to recite the selecting of gene expression level

measurements having a predefined significance score rather than selecting based on its significance score. Claim 27 is further amended at lines 16-18 to recite a plurality of parameters and gene expression level measurements rather than a single parameter and measurement. Claim 27 is amended for clarity beginning at line 19 to recite: “a module determining the non-overlapping parameter(s) present in the selected gene expression level measurements but not present in the non-selected gene expression level measurements”. Claim 27 is amended at the end by addition of the phrase: “wherein the function of the gene can be inferred based on the non-overlapping parameters”. Claim 27 is amended throughout to replace the term “said” with the term “the”. Support for these amendments can be found throughout the claims and specification as filed and, in particular, at page 4, lines 6-9; original claim 6; page 3, lines 16-17; page 3, lines 19-23; and page 3, lines 23-24. Accordingly, no impermissible new matter has been added by this claim amendment.

Claim 28 is amended to recite a method of inferring a function of a gene. Claim 28 is amended for clarity by insertion at lines 3 and 6 of the term “gene” in front of the phrase “expression level measurements”. Claim 28 is also amended for clarity at line 6 by insertion of the phrase “each of” in front of “the gene expression level measurements”. Claim 28 is amended at line 5 by insertion of the phrase as follows: “wherein the scores are outputted to a memory”. In addition, claim 28 is amended at line 7 to recite the selecting of samples having a predefined score rather than selecting based on the most significant score. Claim 28 is further amended for clarity beginning at line 8 to recite: “determining the parameters that are non-overlapped between the selected samples and the samples that were not selected”. Support for these amendments can be found throughout the claims and specification as filed and, in particular, at page 4, lines 6-9; original claim 6; page 3, lines 16-17; page 3, lines 19-23. Accordingly, no impermissible new matter has been added by this claim amendment.

Claim 29 is amended at line 6 by insertion of the phrase as follows: “wherein the significance scores are outputted to a memory”. In addition, claim 29 is amended at line 7 to recite the selecting of data points having a predefined significance score rather than selecting based on its significance score. Claim 29 is further amended for clarity beginning at line 9 to recite “comparing at least one of the parameters between the

selected and the non-selected data points”. Claim 29 is amended for clarity beginning at line 12 to recite: “to determine the non-overlapping parameter(s) present in the selected data points but not present in the non-selected data points”. Claim 29 is amended at the end by addition of the phrase: “wherein the function of the biological molecule can be inferred based on the non-overlapping parameters”. Claim 29 is amended throughout to replace the term “said” with the term “the”. Support for these amendments can be found throughout the claims and specification as filed and, in particular, at page 4, lines 6-9; original claim 6; page 3, lines 16-17; page 3, lines 19-23; and page 3, lines 23-24. Accordingly, no impermissible new matter has been added by this claim amendment.

III. Response to Objections to the Claims

Claim 28 is objected to for allegedly being grammatically incorrect. Claim 28 is herein amended by changing the term “sample” at line 10 to recite “samples” instead. Accordingly, the objection is believed to be obviated by amendment.

IV. Response to the Rejections under 35 U.S.C. § 101

Claims 1-30 are rejected under 35 U.S.C. § 101 for allegedly failing to recite a tangible result.

Initially, as noted hereinabove, applicants respectfully submit that claims 6, 9, 15, 23, 26, and 30 have been canceled herein without prejudice or acquiescence, thereby rendering the rejection of claims 6, 9, 15, 23, 26, and 30 moot.

Independent claims 1, 10, 18, 27-29 are herein amended by addition of a phrase reciting “wherein the scores are outputted to a memory”. Accordingly, Applicants respectfully assert that the rejection under 35 U.S.C. § 101 is overcome, and respectfully request that the rejection of claims 1-5, 7, 8, 10-14, 16-22, 24, 25, and 27-29 under 35 U.S.C. § 101 be withdrawn.

V. Response to the Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-30 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter. Applicants respectfully disagree with the § 112 rejections and submit that the original claims are not unclear, as one of ordinary skill in the art would understand what is meant by the claims. However, in order to facilitate prosecution of the application, the claims are herein amended as follows.

Initially, applicants respectfully submit that, without acquiescing to the rejection, claims 6, 9, 15, 23, 26, and 30 have been canceled herein, thereby rendering the rejection of claims 6, 9, 15, 23, 26, and 30 moot.

Independent claims 1, 10, 18, 27, and 29 are amended to recite a nexus between the preamble and the final step of the claim by addition of the phrase “wherein the function of the gene can be inferred based on the non-overlapping parameters” (claims 1, 10, 18, and 27) or “wherein the function of the biological molecule can be inferred based on the non-overlapping parameters” (claim 29).

In addition, the term “its” has been deleted by amendment from claims 1, 10, 18, 27, and 29. Claims 1, 10, 18, 27, and 29 have been amended to clarify the wording of the step involving comparing/determining a non-overlapping parameter. As a result of amendments to claims 1-25, there is sufficient antecedent basis for the phrase “the gene expression level measurements” which occurs in claims 2, 3, 5, 6, 8, 11, 12, 14, 15, 17, 19, 20, 22, 23, and 25. Claim 18 has been amended to correct the typographical error of using the term “method” rather than “system”. Claim 28 has been amended for clarity by insertion of the phrase “each of” in front of “the expression level measurements”. Claim 29 is amended for clarity by replacement of the term “the” with “a” in front of “function” in the preamble. Accordingly, Applicants respectfully submit that the § 112, second paragraph, rejection of claims 1-5, 7, 8, 10-14, 16-22, 24, 25, and 27-29 has been overcome and request withdrawal of the rejection of claims 1-5, 7, 8, 10-14, 16-22, 24, 25, and 27-29 under 35 USC § 112, second paragraph.

VI. Response to the Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-30 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. In particular, the Patent Office contends that one of skill in the art would not be able to infer the function of a gene without considerable additional research and that, even then, such function determination is unpredictable. The Patent Office cites U.S. Patent Publication No. 2003/0068649 to Doberstein et al. (hereinafter "Doberstein") to support that there are numerous difficulties involved in relating gene sequences to other factors. Thus, the Patent Office contends that one of skill in the art would not conclude that simply comparing genotypes results in inferring the function of a gene.

Applicants respectfully traverse the rejection and offer the following remarks.

Initially, without acquiescing to the rejection, applicants respectfully submit that claims 6, 9, 15, 23, 26, and 30 have been canceled herein, thereby rendering the rejection of claims 6, 9, 15, 23, 26, and 30 moot.

Applicants respectfully submit that the burden rests upon the Patent Office to establish a *prima facie* case of a failure to comply with 35 U.S.C. § 112, first paragraph. See *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1971). There are many factors to be considered when making the determination as to whether an application has met the requirements for enablement under 35 U.S.C. § 112, first paragraph, and whether any necessary experimentation is undue, these factors including: (a) the breadth of the claims, (b) the nature of the invention, (c) the state of the prior art, (d) the level of ordinary skill in the art, (e) the level of predictability in the art, (f) the amount of direction provided by the inventor, (g) the existence of working examples, and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) and Manual of Patent Examining Procedure (hereinafter "MPEP") § 2164.01(a).

Further, applicants respectfully submit that to fulfill the enablement requirement of 35 U.S.C. § 112, first paragraph, it is not necessary to enable one of skill in the art to make and use a perfected, commercially viable embodiment. See MPEP § 2164, citing *CFMT, Inc., v. Yieldup Int'l Corp.*, 349 F.3d, 1333, 1338, 68 USPQ2d 1940, 1944 (Fed.

Cir. 2003). In addition, with regard to experimentation, applicants respectfully submit that a “considerable amount of experimentation is permissible, if it is merely routine.” See MPEP § 2164.06, citing *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976)).

Applicants respectfully submit that, contrary to the Patent Office’s assertion, the presently disclosed and claimed subject matter does not simply relate to comparing genotypes. Applicants respectfully submit that the currently pending claims relate to methods, systems, and computer readable medium for determining the function of a gene or a biological molecule (e.g., a protein) using a distribution of data measurements, such as expression level measurements, obtained for that particular gene or biological molecule over a variety of experimental parameters. The experimental parameters can include ecotype, tissue, RNA type, harvest conditions, genotype, growth conditions, growth media, treatments, etc. See Instant Specification, page 7, lines 12-13. Each data measurement in the distribution is given a significance score as determined via an appropriate statistical method. See Instant Specification, page 3, lines 5-6. The measurements having a predefined score are selected and the experimental parameters associated with the selected measurements are compared to those associated with the non-selected measurements. See Instant Specification, page 3, lines 16-23. The “non-overlapping” parameters, i.e., the parameters associated with the selected measurements but not with the non-selected measurements, are then used to infer function to the gene or biological molecule. See Instant Specification, page 3, lines 23-24. Applicants respectfully submit that steps, means, or modules relating to the assembling or accessing of a data distribution, the calculating of significance scores, the selecting of data measurements, and the comparing of parameters are present in each of independent claims 1, 10, 18, and 27-29.

In particular, applicants note that the presently disclosed methods relate to comparing data measurements relating to one gene or one biological molecule at a time. See, e.g., Instant Specification, page 7, lines 13-14, which recites that the distribution of expression levels over the parameter space is obtained for a given gene. The methods can be used to infer the function of more than one gene or molecule by

repeating the entire process for each gene or molecule being studied. See Instant Specification, page 9, line 14.

The instant specification describes an example wherein the function of a gene from *Arabidopsis* (i.e., rock cress) is inferred using gene expression levels measured in *Arabidopsis* grown under differing growing conditions and where the gene expression is measured in different plant tissues. Based upon the data, it was determined that light treatment is a significant factor in gene expression level, inferring that there is a significant chance that the gene operates with a circadian cycle. See Instant Specification, page 8, line 1 to page 9, line 13.

As noted hereinabove, the Patent Office cites Doberstein as pointing out difficulties in relating gene sequences to other factors. However, it appears that Doberstein describes difficulties that can be encountered when attempts are made to determine the function of a gene by comparing it to another gene or because of difficulties encountered in various expression systems. For example, Doberstein paragraph [0004] appears to take the position that sequence data alone is not enough to infer that a particular DNA sequence has a similar function to another DNA sequence just because they have similar sequences. Applicants respectfully submit that the difficulties described in Doberstein would not relate to the presently described methods wherein gene function is determined by comparing multiple gene expression data measurements for a single gene over a variety of parameters and determining which parameters are significant to gene expression.

The Patent Office further alleges that it is possible that some gene expression measurements are significant due to experimental noise in the data. Applicants respectfully submit that the subject specification specifically describes a variety of suitable statistical methods that can be used (see Instant Specification, page 9, line 24 to page 10, line 1) and notes that the statistical methodology should operate to generate criteria to separate and group at least one member from the group. See Instant Specification, page 10, lines 2-4. Applicants respectfully submit that, particularly after a review of the subject application, one of skill in the art would be able to determine the proper statistical method and a proper sample size in order to overcome any problems relating to experimental noise.

Accordingly, applicants respectfully submit that the presently claimed subject matter of inferring a function of a gene or biological molecule is believed to meet the enablement requirement of 35 U.S.C. § 112, first paragraph. Applicants respectfully request that the rejection of claims 1-5, 7, 8, 10-14, 16-22, 24, 25, and 27-29 under 35 USC § 112, first paragraph, be withdrawn and further ask that claims 1-5, 7, 8, 10-14, 16-22, 24, 25, and 27-29 be allowed at this time.

VII. Response to the Rejections under 35 U.S.C. § 102

Claims 1-3, 6-12, 15-20, and 23-30 have been rejected under 35 U.C.S. § 102(a) as allegedly being anticipated by journal article to Van der Laan et al. (*Biostatistics*, December 2001, Vol. 2(4): pages 445-461; hereinafter "Van der Laan"). Applicants respectfully traverse the rejections under § 102(a).

Initially, applicants respectfully submit that claims 6, 9, 15, 23, 26, and 30 have been canceled without acquiescence herein, thereby rendering the rejection of claims 6, 9, 15, 23, 26, and 30 moot.

Applicants respectfully submit that claims 1, 10, 18, and 27 have each been amended herein to recite "assembling a distribution of gene expression level measurements for a given gene over a variety of experimental conditions." Claim 28 has been amended to recite the method of inferring a function of "a gene" by "accessing multiple gene expression level measurements for multiple samples collected under diversified conditions defined by parameters corresponding to the gene."

Thus, as noted hereinabove, applicants respectfully submit that the presently claimed methods, systems, and computer readable medium relate to comparing multiple data measurements (e.g., multiple gene expression level measurements) from the same gene (or biological molecule). See also, Instant Specification, page 7, lines 13-14, which recites that "[t]he distribution of the expression levels over the parameter space is obtained for a given gene." The parameters can correspond to experimental conditions. See Instant Specification, page 3, line 3. Thus, for example, gene expression level measurements that have a predefined significance score are selected from a distribution and the "non-overlapping" parameters, i.e., the parameters associated with the selected gene expression levels but not with the non-selected gene

expression levels, are used to infer function to the gene. For instance, as described in the example related to *Arabidopsis* gene expression data, it is determined that light treatment is a significant factor in gene expression level, inferring that there is a significant chance that the gene operates with a circadian cycle. See Instant Specification, page 8, line 1 to page 9, line 13. Each of claims 1, 10, 18, 27, 28, and 29 recite that the function of a gene or biological molecule is inferred based on non-overlapping parameters.

Applicants respectfully submit that Van der Laan does not appear to use varying expression of a particular (i.e., a single) gene or molecule under differing experimental conditions to infer function of the basis of non-overlapping parameters. Rather, applicants respectfully submit that Van der Laan appears to at best describe a method in which expression levels of genes are compared to expression levels of other genes in order to determine function. For example, at page 447, first full paragraph, Van der Laan recites interest in “genes whose expression levels tend to vary together, because such genes might be part of the same causal mechanism.”

Accordingly, applicants respectfully submit that claims 1, 10, 18, 27, 28 and 29 have been distinguished from Van der Laan. As claims 2, 3, 7, 8, 11, 12, 16, 17, 19, 20, 24, and 25 each depend from one of claims 1, 10, and 18, applicants respectfully submit that claims 2, 3, 7, 8, 11, 12, 16, 17, 19, 20, 24, and 25 are each also distinguished from Van der Laan. Applicants respectfully request that the rejection of claims 1-3, 7, 8, 10-12, 16-20, 24, 25, and 27-29 under 35 U.S.C. § 102 (a) in view of Van der Laan be withdrawn and ask that claims 1-3, 7, 8, 10-12, 16-20, 24, 25, and 27-29 be allowed at this time.

VIII. Response to the Rejections under 35 U.S.C. § 103(a)

Claims 1-30 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Van der Laan in view of U.S. Patent Application Publication No. 2003/0219797 to Zhao et al. (hereinafter “Zhao”). In particular, the Patent Office contends that Van der Laan does not describe that the significance score is a z-score or that the z-score is greater than 3 and less than -3. The Patent Office alleges that Zhao

describes statistically analyzing large data arrays and using a significant z-score of 4.8 or higher.

Applicants respectfully traverse the rejections and the Patent Office's comments and offer the following remarks.

Initially, applicants respectfully submit that claims 6, 9, 15, 23, 26, and 30 have been canceled without acquiescence herein, thereby rendering the rejection of claims 6, 9, 15, 23, 26, and 30 moot.

Further, applicants respectfully submit that it is believed that Zhao is being cited for its recitation of z-scores. Zhao does not overcome the deficiencies of Van der Laan with regard to claims 1, 10, 18, and 27-29 and their dependent claims, as described hereinabove.

Accordingly, applicants respectfully submit that Van der Laan and Zhao, alone or in combination, do not teach or suggest assembling, a means of assembling, or a module for assembling a distribution of gene expression level measurements for a given gene over a variety of experimental conditions, as recited in claims 1, 10, 18, and 27. Nor does the cited combination teach a method of inferring a function of a gene comprising accessing multiple gene expression level measurements for multiple samples collected under diversified conditions defined by parameters corresponding to the gene as recited in claim 28. Finally, the cited combination does not teach or suggest a method, system or computer readable medium wherein the function of a gene or biological molecule can be inferred based on non-overlapping parameters as recited in claims 1, 10, 18, 27, 28, and 29.

Accordingly, applicants respectfully ask that the rejection of claims 1-5, 7, 8, 10-14, 16-22, 24, 25, and 27-29 under 35 U.S.C. § 103(a) in view of Van der Laan and Zhao be withdrawn and ask that claims 1-5, 7, 8, 10-14, 16-22, 24, 25, and 27-29 be allowed at this time.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

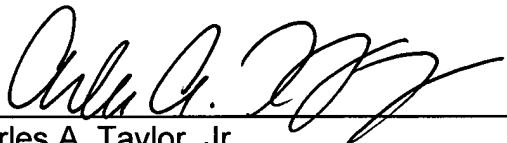
The Commissioner is hereby authorized to charge any deficiencies of payment or credit any overpayment associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,

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